

may be caused by structural epidermal defects. Late stage *shd* mutants display global defects in epidermal keratinocytes. *shd* epidermis at e18.5 is dramatically thickened, hyperproliferative, and poorly differentiated, encasing the mutants in an epidermal cocoon. The *shd* phenotype is similar to animals with mutations in *IKKalpha*, *interferon regulatory factor 6*, or *stratifin* suggesting that they may act together to control proliferation and differentiation of skin keratinocytes. Studying the interactions between these genes will enhance our understanding of the pathways regulating epidermal integrity, expansion, and differentiation throughout development.

doi:[10.1016/j.ydbio.2009.05.086](https://doi.org/10.1016/j.ydbio.2009.05.086)

Program/Abstract # 71

Insights into the organization of dorsal spinal cord pathways from an evolutionarily-conserved *Raldh2* (*Aldh1a2*) intronic enhancer

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Dorsoventral organization of the vertebrate spinal cord into sensory, motor and integrative domains is mediated by Sonic hedgehog from the notochord/floor plate and Bmp, Wnt and retinoic acid (RA) from the roof plate. We describe an intronic enhancer of the *raldh2* gene that encodes the RA synthetic enzyme, RALDH2/ALDH1A2. This dorsal spinal cord enhancer is conserved in tetrapods, but absent from teleosts. Studies in frogs, mice and chicken revealed enhancer activity in the spinal cord roof plate and in dorsal-most interneurons. Activation in dorsal-most interneurons and reporter expression in cell bodies and axons of commissural interneurons suggests roles in the ontogeny of circuits conveying proprioceptive information to the cerebellum and to the contralateral spinal cord. Interestingly, *raldh2* is expressed in the embryonic dorsal spinal cord of the primitive agnathan *Petromyzon marinus*, consistent with an ancestral role of RA signaling in vertebrate spinal cord dorsoventral patterning.

doi:[10.1016/j.ydbio.2009.05.087](https://doi.org/10.1016/j.ydbio.2009.05.087)

Program/Abstract # 72

Characterization of a genetic network sufficient to convert cells to functional eyes

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The vertebrate eye develops from a single field of neuroectodermal cells in the anterior neural plate called the eye field. This region is required and sufficient for eye formation. Work in a variety of model systems demonstrates that a group of transcription factors (EFTFs) are coordinately expressed in the eye field and essential for normal eye formation. We took advantage of the relatively simple *Xenopus laevis* animal cap system to address two questions: "Can EFTFs re-program cells to form a functional eye?", and "What are the downstream targets of the EFTFs required for normal eye formation?" When cultured in isolation, then transplanted to developing embryos, animal cap cells differentiated into epidermis. In contrast, EFTF expressing cells formed eyes that were molecularly and anatomically similar to normal eyes. Importantly, induced eyes could guide a vision-based behavior. Using this unique tool, we developed a microarray-based strategy to identify genes expressed during the early stages of eye formation. We have identified over 300 transcripts regulated in the endogenous eye field and in cells directed to an eye

field-like fate. Many of the most highly induced transcripts coded for genes required for normal eye formation in flies, frogs, mice and/or humans. We also identified evolutionarily conserved, novel genes that were expressed in the eye field. These results suggest the *Xenopus* transcriptosome required for eye formation will be a valuable tool for cross species comparisons, identification of new genes, and the generation of a preliminary map of the genetic network driving early eye formation.

doi:[10.1016/j.ydbio.2009.05.088](https://doi.org/10.1016/j.ydbio.2009.05.088)

Program/Abstract # 73

Macro- and micro-environmental regulation of ectodermal organ stem cells

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We develop further the concept of 1) environmental regulation of stem cell activities and 2) topobiological arrangement of stem cells and organ shape. We propose that throughout the duration of an organism's life, skin appendage stem cells are modulated by a combination of micro-environmental factors and macro-environmental factors to regulate its regenerative cycles, and to shape its morphology. We use feather morphogenesis to study micro-environmental regulation of stem cell topology. Feather stem cells are configured in a ring shape at the bottom of the follicle. We demonstrate that topobiological arrangements of stem cells, TA cell and differentiated cells are key to the shape of feather branches. The environments are controlled by the dermal papilla. We also show how stem cells are patterned during feather induction. The beta catenin positive, homogeneous stem cells in the feather field (basal states) are organized into hexagonally-arranged placodes (state A) and inter-bud space (state B). We explore the role of a Turing reaction-diffusion mechanism in establishing chemical patterns. We use regenerative hair wave to illustrate macro-environmental regulation. We show there is oscillation of dermal Bmp signaling which is asynchronous with hair cycling. The interactions of these two rhythms lead to the recognition of refractory and competent phases in the telogen, and autonomous and propagating phases in the anagen. Bmp2 expression in subcutaneous adipocytes gives implications in Evo-Devo. We further explore the hair wave in compound follicles in other mammals.

doi:[10.1016/j.ydbio.2009.05.089](https://doi.org/10.1016/j.ydbio.2009.05.089)

Program/Abstract # 74

The novel actin nucleator Cordon-bleu interacts with Syndapins during epithelial development

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The molecular coordination of intercellular patterning signals to cell shape changes and tissue morphogenesis is not well understood. Here we present evidence that Cordon-bleu (Cobl) may function in this capacity. *Cobl* is a novel mouse gene that is expressed initially in the axial midline, and later in several developing epithelial tissues. In the neural tube, *Cobl* expression is positively regulated by Shh and negatively regulated by BMP signaling. A hypomorphic allele of *Cobl* interacts with mutations in *Vangl2*, a member of the planar cell polarity pathway, to cause defective midbrain neural tube closure, demonstrating a role for both genes in midbrain neurulation. *Cobl* is apically localized in epithelial cells such as the floorplate, where it closely localizes with F-actin. Molecular studies show that *Cobl*'s

three WH2 domains bind monomeric actin and are able to nucleate new actin filaments in vitro. A yeast two-hybrid screen demonstrated that Cobl also binds the Syndapin (Sdp) family of proteins, which link the processes of endocytosis with actin cytoskeleton remodeling. Cobl and Sdp2 are expressed in the same tissues in the developing embryo and colocalize at the cell cortex in cultured epithelial cells. Knockdown of Cobl in epithelial cells leads to a reduction of Sdp2 protein at the membrane. Conversely, knockdown

of Sdp2 does not alter localization of Cobl. These data suggest that Cobl recruits Sdp2 to the cell cortex where they may function together. Further molecular studies are investigating the role of this interaction on endocytosis and actin cytoskeletal remodeling during epithelial development.

doi:[10.1016/j.ydbio.2009.05.090](https://doi.org/10.1016/j.ydbio.2009.05.090)
